

Dental prophylaxis decreases the risk of acute myocardial infarction: a nationwide population-based study in Taiwan

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Purpose: To investigate the association between periodontal disease (PD) and acute myocardial infarction (AMI), and evaluate the effect of dental prophylaxis on the incidence rate (IR) of AMI.

Methods: The Longitudinal Health Insurance Database 2000 from the National Health Insurance program was used to identify 511,630 patients with PD and 208,713 without PD during 2000–2010. Subjects with PD were grouped according to treatment (dental prophylaxis, intensive treatment, and PD without treatment). The IRs of AMI during the 10-year follow-up period were compared among groups. Cox regression analysis adjusted for age, sex, socioeconomic status, residential urbanicity, and comorbidities was used to evaluate the effect of PD treatment on the incidence of AMI.

Results: The IR of AMI among subjects without PD was 0.19%/year. Among those with PD, the IR of AMI was lowest in the dental prophylaxis group (0.11%/year), followed by the intensive treatment (0.28%/year) and PD without treatment (0.31%/year; $P < 0.001$) groups. Cox regression showed that the hazard ratio (HR) for AMI was significantly lower in the dental prophylaxis group (HR = 0.90, 95% confidence interval = 0.86–0.95) and higher in the intensive treatment (HR = 1.09, 95% confidence interval = 1.03–1.15) and PD without treatment (HR = 1.23, 95% confidence interval = 1.13–1.35) groups than in subjects without PD.

Conclusion: PD is associated with a higher risk of AMI, which can be reduced by dental prophylaxis to maintain periodontal health.

Keywords: periodontal disease, acute myocardial infarction, dental prophylaxis, dental scaling

Introduction

Coronary heart disease (CHD) is the leading cause of morbidity and mortality worldwide, with a prevalence ranging from 2%–20%.^{1,2} Acute myocardial infarction (AMI) is a CHD-related event that may result in sudden death. The risk factors for CHD include age, male sex, hypertension, diabetes mellitus, dyslipidemia, smoking, and inflammatory diseases, such as periodontal disease (PD).^{3–6}

About 20%–50% of the population worldwide has PD.^{7–9} This disease is caused by the accumulation of a specific bacterial biofilm around teeth. The initial presentation is reversible gingivitis, which can be treated after biofilm removal.^{10–12} As PD progresses, destruction of the periodontal connective tissue and alveolar bone ultimately lead to tooth loss.¹³ Increased tooth brushing frequency has been found to reduce the serum concentrations of C-reactive protein and fibrinogen, suggesting that the improvement of periodontal conditions can reduce a patient's systemic inflammatory status.¹⁴

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Some previous researchers have concluded that poor periodontal status is associated with an increased risk of CHD.^{13,15–18} Deep periodontal pockets have been found in individuals who have experienced AMI and have been associated with an increased incidence of this event.^{19–21} A larger variation of subgingival anaerobic microflora has also been observed in those who have experienced AMI and is considered to be a potential risk indicator.^{22,23} However, other reports showed no significant relationship between PD and CHD.^{24,25} The relationships of PD and its treatment with the incidence of AMI remain unclear.

A retrospective cohort study was conducted using the Taiwanese National Health Insurance Research Database (NHIRD) to estimate the incidence rates (IRs) of AMI among subjects with PD and different PD treatment groups.

Methods

This study received full review by the local institutional review board (Taipei City Hospital Institutional Review Board number: TCHIRB-1020705-E). The institutional review board waived the need for written informed consent from study subjects because all potentially patient-identifying information was encrypted.

Data source

The compulsory, universal National Health Insurance (NHI) program in Taiwan covers up to 99% of the nation's inhabitants. In conjunction with the NHI Bureau, the National Health Research Institute established the NHIRD to provide useful epidemiological information for basic and clinical research in Taiwan. The National Health Research Institute administers the NHIRD in a manner that ensures all beneficiaries' privacy and confidentiality, and provides access to researchers only upon ethical approval.

For this study, the Longitudinal Health Insurance Database 2000 (LHID 2000) was used. The LHID 2000 is a standardized sample file for research use provided by the National Health Research Institute, and consists of comprehensive use and enrollment information for a randomly selected sample of 1 million NHI beneficiaries, representing approximately 5% of all enrollees in Taiwan in 2000. A multistage stratified systematic sampling design was used and it was found that there were no statistically significant differences in sex or age between the sample group and all enrollees. The identification of patients in the LHID 2000 is encrypted to protect their privacy, as this database includes information about medical orders, treatment procedures, and medical diagnoses (coded based on the *International*

Classification of Diseases, 9th Revision, Clinical Modification [ICD-9-CM]).

Study cohort

The cohort for this retrospective study was drawn from 1 million beneficiaries sampled randomly from all beneficiaries listed in the NHIRD in the year 2000 (ie, the LHID 2000). Only subjects aged ≥ 20 years were included (723,024 beneficiaries; Figure 1). The subjects were included into the PD cohort if they visited an ambulatory care provider due to PD (ICD-9-CM codes 523.0–523.5) during the study period. Patients who developed AMI before PD diagnosis ($n=2,066$) and individuals of unknown sex ($n=615$) were excluded. Individuals with no diagnosis of PD from 2000–2010 served as the control group ($n=208,713$; followed for 2,248,618 person-years).

The PD group (ICD-9-CM codes 523.0–523.5) was divided into three treatment groups:

- 1) Dental prophylaxis ($n=344,228$; followed for 2,807,865 person-years): PD patients who only received dental prophylaxis (procedure codes: 91003, 91004) during the following period.
- 2) Intensive treatment ($n=121,827$; followed for 789,518 person-years): PD patients who received treatments such as subgingival curettage and root planning (procedure codes: 91006–91008) and/or periodontal flap operation (procedure codes: 91009, 91010) and/or tooth extraction (procedure codes: 92013, 92014).
- 3) PD without treatment ($n=45,575$; followed for 170,754 person-years): PD patients who received no treatments.

Thus, a total of 720,343 subjects followed for 6,016,755 person-years were included in this study. Participants were followed from the cohort entry date (the first date of an ambulatory care visit due to PD for the PD group and January 1, 2000 for the control group) until the date of hospitalization due to AMI (ICD-9-CM codes 410–412), death, or end of the study period (December 31, 2010).

The socioeconomic status variable had five categories. People with a well-defined monthly payroll were classified into three categories: \geq NT\$40,000, NT\$20,000–\$39,999, and $<$ NT\$20,000 (NT\$: New Taiwan dollars; US\$1 is approximately worth NT\$30). People without a well-defined monthly wage could either enroll through unions or associations, such as farmers' associations, or through local government offices. Those who enrolled through local government offices included self-employed, retirees, corner store owners, or low-income people. People without a well-defined monthly payroll were categorized into two groups:

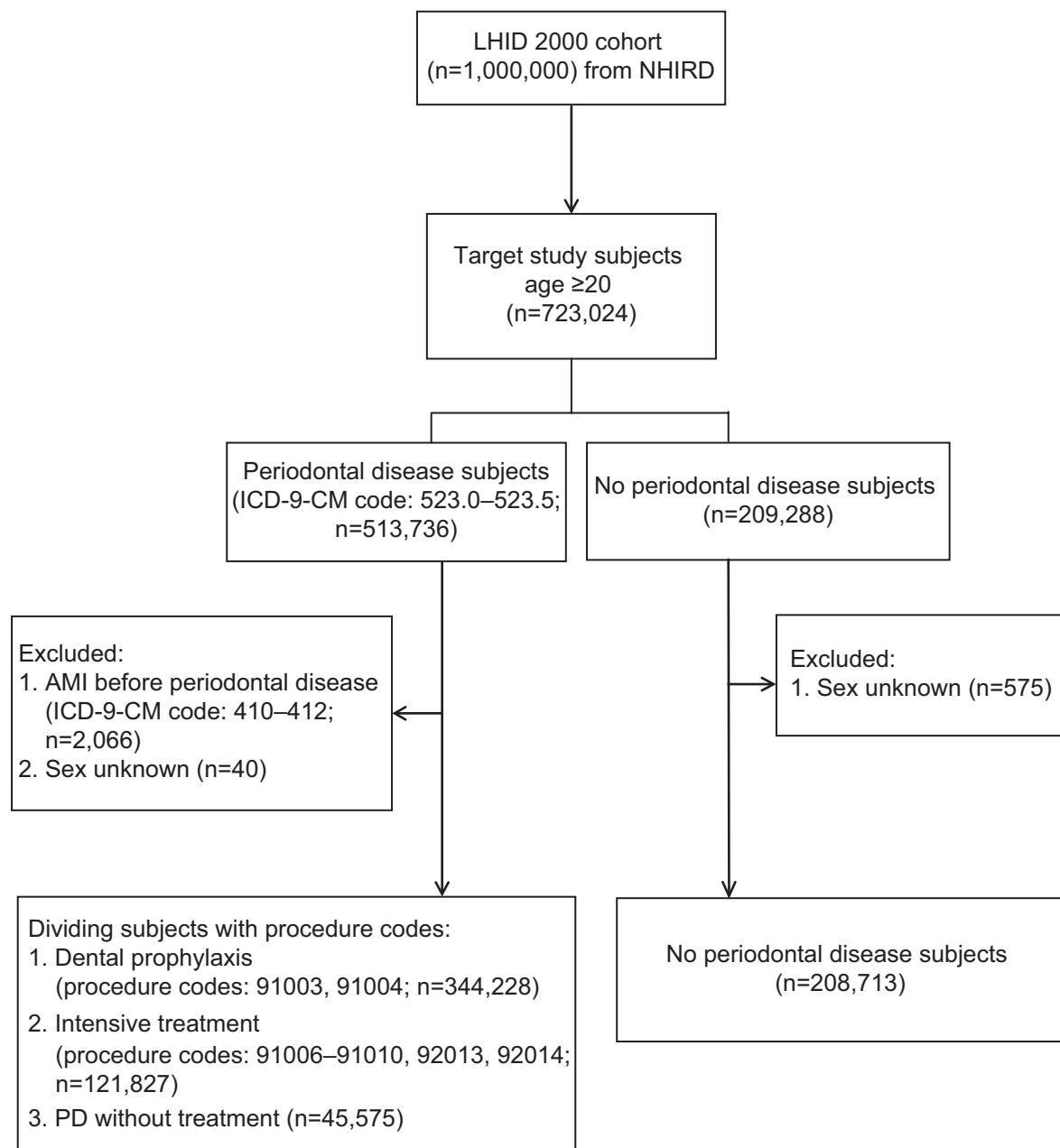


Figure 1 Selection of study patients.

Abbreviations: AMI, acute myocardial infarction; ICD-9-CM, *International Classification of Diseases, 9th Revision, Clinical Modification*; LHID, Longitudinal Health Insurance Database; NHIRD, National Health Insurance Research Database; PD, periodontal disease.

union or association members and people enrolled in local government offices.

The residential urbanicity was classified into three categories: urban classification for metropolitan cities; suburban classification for all other cities and counties; and rural classification for all townships and rural areas.

In the analysis of AMI comorbidities, including atrial fibrillation (ICD-9-CM code 437.3), diabetes (ICD-9-CM code 250), hypertension (ICD-9-CM codes 401–405), dyslipidemia (ICD-9-CM code 272), chronic kidney disease

(ICD-9-CM code 585), and peripheral vascular disease (ICD-9-CM codes 440.2, 440.3, 440.9, 443, 444.21, 444.22), only subjects with more than three outpatient visits during the study period were included to increase the validity of diagnoses in the administrative data set.

Statistical methods

Statistical analyses were performed using the SAS® statistical package (version 9.2; SAS Institute, Cary, NC, USA). The IRs of AMI among patients with PD and control

subjects were compared. The χ^2 test was used for parametric categorical data. A *P*-value of less than 0.05 was considered significant. A Cox proportional hazards model was used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) to determine whether PD is a risk factor for the development of AMI. This model was adjusted for age, sex, socioeconomic status, residential urbanicity, PD treatment, and comorbidities (atrial fibrillation, diabetes mellitus,

hypertension, dyslipidemia, chronic kidney disease, and peripheral vascular disease).

Results

A total of 10,046 patients developed AMI during the follow-up period (IR =0.17%/year; Table 1). The IR of AMI increased with age from 0.03%/year among subjects aged 20–44 years to 0.24% and 0.61%/year among those aged

Table 1 Univariate analysis of factors affecting the incidence of acute myocardial infarction

Variables	Total (n)	AMI (n)	Follow-up (person-years)	IR (%/year)	χ^2 test (P-value)
Total	720,343	10,046	6,016,755	0.17	
Age at baseline					<0.001
20–44 years	436,383	1,032	3,622,234	0.03	
45–64 years	186,875	3,633	1,506,826	0.24	
≥65 years	97,085	5,381	887,695	0.61	
Sex					<0.001
Female	352,249	3,689	2,927,932	0.13	
Male	368,094	6,357	3,088,823	0.21	
Socioeconomic status					<0.001
<NT\$20,000	194,532	1,743	1,777,477	0.10	
NT\$20,000–39,999	179,369	1,552	1,397,611	0.11	
≥NT\$40,000	128,113	1,463	1,020,913	0.14	
Union/association member	103,075	2,813	870,662	0.32	
Local government enrollees	115,254	2,475	950,093	0.26	
Residential urbanicity					<0.001
Urban	434,975	5,308	3,594,699	0.15	
Suburban	220,457	3,320	1,866,215	0.18	
Rural	64,911	1,418	555,841	0.26	
Periodontal disease					<0.001
No PD	208,713	4,327	2,248,618	0.19	
Dental prophylaxis	344,228	2,952	2,807,865	0.11	
Intensive treatment	121,827	2,233	789,518	0.28	
PD without treatment	45,575	534	170,754	0.31	
Comorbidity					
Atrial fibrillation					<0.001
No	714,085	9,594	5,965,271	0.16	
Yes	6,258	452	51,484	0.88	
Diabetes					<0.001
No	638,060	6,406	5,355,794	0.12	
Yes	82,283	3,640	660,962	0.55	
Hypertension					<0.001
No	544,877	3,072	4,603,550	0.07	
Yes	175,466	6,974	1,413,206	0.49	
Dyslipidemia					<0.001
No	605,948	6,755	5,117,645	0.13	
Yes	114,395	3,291	899,110	0.37	
CKD					<0.001
No	708,023	9,158	5,914,168	0.15	
Yes	12,320	888	102,587	0.87	
PVD					<0.001
No	706,158	9,452	5,902,939	0.16	
Yes	14,185	594	113,816	0.52	

Note: US\$1 is approximately worth NT\$30.

Abbreviations: AMI, acute myocardial infarction; CKD, chronic kidney disease; IR, incidence rate; NT\$, New Taiwan dollar; PD, periodontal disease; PVD, peripheral vascular disease.

45–64 years and >65 years, respectively ($P < 0.001$). The IR of AMI was higher among men than women (0.21% versus 0.13%/year) and was significantly higher among subjects with atrial fibrillation (0.88%/year), diabetes mellitus (0.55%/year), hypertension (0.49%/year), dyslipidemia (0.37%/year), chronic kidney disease (0.87%/year), and peripheral vascular disease (0.52%/year) than people without these comorbidities (all $P < 0.001$).

A total of 4,327 people without PD developed AMI (IR = 0.19%/year). Among those with PD, the IR of AMI was lowest in the dental prophylaxis group (0.11%/year) and highest in the PD without treatment group (0.31%/year; $P < 0.001$).

When comparing IRs of AMI after being stratified by age, sex, socioeconomic status, residential urbanicity, and comorbidity variables (Table 2), the lowest IR of the PD population always appeared in the dental prophylaxis group, followed by the intensive treatment group and PD without treatment group ($P < 0.001$ or $P = 0.013$ for the trend test).

Cox regression analysis adjusted for age, sex, socioeconomic status, residential urbanicity, and comorbidities showed that the HR of AMI was significantly lower in the dental prophylaxis group (HR = 0.90, 95% CI = 0.86–0.95) and higher in the intensive treatment (HR = 1.09, 95% CI = 1.03–1.15) and PD without treatment (HR = 1.23, 95% CI = 1.13–1.35) groups than among subjects with no PD (Table 3). The r^2 correlate of the Cox regression model was 2.38%.

Discussion

This is the first nationwide, population-based study to examine the strength of association between periodontal treatment and the incidence of AMI. The results of this study demonstrated that PD is a significant risk factor for AMI, and that dental prophylaxis protects against AMI development.

The findings support the concept that inflammatory diseases such as PD may play a role in the pathogenesis of AMI. The association of PD with the prevalence of CHD suggests that inflammation may be a potential mechanism involved in the regulation of the atherosclerotic process.^{26,27} PD may induce immune cells to secrete the inflammatory cytokines thromboxane A₂, interleukin 1 β , prostaglandin E₂, and tumor necrosis factor α , which trigger and exacerbate atherogenic and thromboembolic processes, resulting in CHD.^{26,28–30} Poor periodontal condition was also reported to be associated significantly with an increased concentration of C-reactive protein,^{31–34} a well-studied inflammatory marker and an independent predictor of CHD.^{35,36} In addition to

circulating inflammatory factors, oral microbial organelles circulating in the blood have been proposed to lead to the increased incorporation of PD pathogens in atherosclerotic plaque.^{26,37} The attached PD pathogens can then adhere to vascular cells, inducing vascular infection and atherothrombosis and eventually causing AMI.³⁸

The HRs among the different PD treatment groups were statistically significantly different. Sometimes this can be due to the very huge sample size used. However, the authors believe that the difference of HR among PD treatment groups had clinical significance. Other different approaches to PD-related conditions also showed a similar finding in the association with AMI. The National Health and Nutrition Examination Survey III cohort study found that patients with severe PD had a four-fold higher risk of myocardial infarction than those without PD.³⁹ Infections of dental origin have also been documented in patients experiencing myocardial infarction.⁴⁰ Periodontal pocket depth has been reported to be associated with the IR of AMI.^{19,20} Tooth loss, an indicator of PD history, was significantly related to carotid intima-media thickness, a strong predictor of myocardial infarction and stroke.^{37,41} Treatment of PD resulting in a beneficial effect on vascular diseases such as AMI and stroke was also reported.^{42–44} The results of a cross-sectional randomized clinical study suggested that nonintensive, Phase I periodontal therapy decreased serum immunoglobulin G and immunoglobulin M levels in patients who developed AMI.⁴² A 7-year cohort study by Chen et al showed that frequent tooth scaling reduced the IR and risk of AMI among subjects aged >50 years.⁴³ In a previous study, it was found that dental prophylaxis reduced the risk of ischemic stroke in subjects with PD, especially those aged 20–44 years.⁴⁴

Several limitations of this study must be considered. First, the use of administrative data and the retrospective design may have resulted in bias with respect to diagnoses. A further concern is the nonresponder bias/selection bias. Although the NHI program in Taiwan covered up to 99% of the nation's inhabitants and provides free dental check-ups and prophylaxis twice a year to promote the prevention of PD, some PD patients may not be included in this NHI database because they did not have health insurance or did not seek treatment or check-up. However, the NHI Bureau routinely samples patient charts in different medical centers to validate database quality and minimize miscoding or misclassification. In addition, patients with PD were identified using both ICD-9-CM diagnostic codes and PD treatment codes in this study to minimize classification errors. Only patients with more than three outpatient visits were included in the analysis

Table 2 Acute myocardial infarction prevalence among study subjects by periodontal disease types

Variables	No PD		Periodontal disease						P-value for trend test				
			Dental prophylaxis			Intensive treatment				PD without treatment			
	AMI (n)	Person-years	IR (%/years)	AMI (n)	Person-years	IR (%/years)	AMI (n)	Person-years		IR (%/years)	AMI (n)	Person-years	IR (%/years)
Age at baseline (years)													
20–44 years	263	1,163,439	0.02	496	2,024,810	0.02	229	350,200	0.07	44	83,785	0.05	<0.001
45–64 years	119	519,597	0.02	1,290	623,262	0.21	970	311,959	0.31	182	52,008	0.35	<0.001
≥65 years	2,873	565,581	0.51	1,166	159,793	0.73	1,034	127,359	0.81	308	34,962	0.88	<0.001
Sex													
Female	1,787	951,092	0.19	1,087	1,546,539	0.07	597	349,999	0.17	218	80,303	0.27	<0.001
Male	2,510	1,297,526	0.19	1,865	1,261,326	0.15	1,636	439,520	0.37	316	90,451	0.35	<0.001
Socioeconomic status													
<NT\$20,000	743	798,879	0.09	541	767,126	0.07	388	175,166	0.22	71	36,306	0.20	<0.001
NT\$20,000–39,999	531	376,425	0.14	567	784,967	0.07	378	195,361	0.19	76	40,858	0.19	<0.001
≥NT\$40,000	453	237,493	0.19	581	599,525	0.10	357	160,270	0.22	72	23,626	0.30	<0.001
Union/association member	1,593	444,929	0.36	600	268,975	0.22	440	117,007	0.38	180	39,750	0.45	<0.001
Local government enrollees	1,007	390,892	0.26	663	387,272	0.17	670	141,715	0.47	135	30,214	0.45	<0.001
Residential urbanicity													
Urban	1,976	1,164,514	0.17	1,751	1,847,309	0.09	1,317	493,400	0.27	264	89,476	0.30	<0.001
Suburban	1,564	794,253	0.20	912	787,166	0.12	675	227,180	0.30	169	57,616	0.29	<0.001
Rural	787	289,851	0.27	289	173,390	0.17	241	68,939	0.35	101	23,662	0.43	<0.001
Comorbidity													
Atrial fibrillation	189	20,378	0.93	130	17,532	0.74	105	11,155	0.94	28	2,418	1.16	0.013
Diabetes	1,416	217,362	0.65	1,081	258,631	0.42	939	157,405	0.60	204	27,564	0.74	<0.001
Hypertension	2,853	486,339	0.59	2,071	571,649	0.36	1,652	294,169	0.56	398	61,048	0.65	<0.001
Dyslipidemia	980	211,397	0.46	1,192	454,098	0.26	937	201,900	0.46	182	31,715	0.57	<0.001
CKD	381	42,828	0.89	243	33,478	0.73	209	21,297	0.98	55	4,985	1.10	<0.001
PVD	211	35,872	0.59	181	47,045	0.38	162	25,388	0.64	40	5,511	0.73	<0.001

Note: US\$ 1 is approximately worth NT\$30.

Abbreviations: AMI, acute myocardial infarction; CKD, chronic kidney disease; IR, incidence rate; NT\$, New Taiwan dollar; PD, periodontal disease; PVD, peripheral vascular disease.

Table 3 Results of Cox regression analysis conducted to identify predictors of acute myocardial infarction development

Variables	HR	95% CI
Age at baseline		
20–44 years	1.00	
45–64 years	4.72	4.39–5.08
≥65 years	9.93	9.21–10.71
Sex		
Female	1.00	
Male	1.66	1.59–1.73
Socioeconomic status		
<NT\$20,000	1.00	
NT\$20,000–39,999	0.97	0.91–1.04
≥NT\$40,000	0.98	0.91–1.05
Union/association member	1.10	1.02–1.18
Local government enrollees	1.17	1.10–1.25
Residential urbanicity		
Urban	1.00	
Suburban	1.01	0.96–1.06
Rural	1.02	0.95–1.09
Periodontal disease		
No PD	1.00	
Dental prophylaxis	0.90	0.86–0.95
Intensive treatment	1.09	1.03–1.15
PD without treatment	1.23	1.13–1.35
Comorbidity		
Atrial fibrillation	1.52	1.38–1.67
Diabetes	1.62	1.55–1.69
Hypertension	2.63	2.50–2.76
Dyslipidemia	1.09	1.04–1.14
CKD	1.60	1.49–1.72
PVD	1.01	0.93–1.10

Note: US\$1 is approximately worth NT\$30.

Abbreviations: CI, confidence interval; CKD, chronic kidney disease; HR, hazard ratio; NT\$, New Taiwan dollar; PD, periodontal disease; PVD, peripheral vascular disease.

of AMI and comorbidities to reduce nondifferential misclassification bias. Second, the lack of information provided by the NHIRD on other risk factors for PD and AMI, such as education, family history, body mass index, and smoking status, could reduce the feasibility and accuracy of the interpretation of analytical outcomes. However, several recent studies have indicated that the significant associations of PD with AMI and recurrent cardiovascular events in patients developing myocardial infarction are independent of smoking status.^{34,45–47} PD has also been demonstrated to contribute to elevated C-reactive protein levels in nondiabetic, nonsmoking patients who have experienced AMI.⁴⁸

Conclusion

The current study demonstrated that PD is correlated with the risk of AMI, and that dental prophylaxis can significantly reduce the IR of AMI. Patients who receive regular prophylactic dental treatment are more likely to have healthier

periodontal conditions and less likely to have systemic chronic inflammatory reactions, resulting in a lower IR of AMI.

Disclosure

The authors report no conflicts of interest in this work. All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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